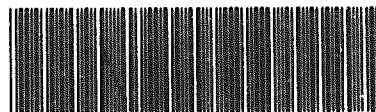


8EHQ-0296-13585  
ORIGINAL

DOW CORNING

February 13, 1996

TSCA Document Control Office (7407)  
Office of Pollution Prevention and Toxics  
US Environmental Protection Agency  
Attn: TSCA 8(e) Coordinator  
401 M Street, S.W.  
Washington, DC 20460



8EHQ-96-13585  
INIT 02/15/96

Re: TSCA Section 8(e) Notification of Substantial Risk  
Octamethylcyclotetrasiloxane (OMCTS)

Dear Sir:

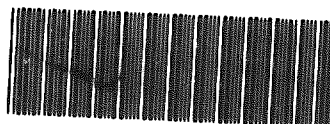
In accordance with the provisions of Section 8(e) of the Toxic Substances Control Act (TSCA), as interpreted in the Statement of Interpretation and Enforcement Policy (40 FR 11110, March 16, 1978), Dow Corning Corporation is submitting the following Notification of Substantial Risk for an ongoing study which we are conducting as part of our siloxane research program, a thirty million dollar voluntary health effects research program on six siloxane materials, a program which has been reviewed with EPA's Office of Pollution Prevention and Toxics on several occasions. The information submitted in this notification is interim data obtained from preliminary range-finding inhalation reproductive studies in Sprague-Dawley rats with octamethylcyclotetrasiloxane (OMCTS, D<sub>4</sub>). While we do not believe the results of these preliminary range finding studies represent a substantial risk to health or environment, we are nevertheless, reporting them to EPA to assure our compliance with the letter and spirit of TSCA Section 8(e).

**Chemical Substance:**

556-67-2 Octamethylcyclotetrasiloxane

**Manufacturer:**

Dow Corning Corporation  
2200 West Salzburg Road  
Midland, Michigan 48686-0994



88960000065

**Ongoing Studies:**

INHALATION REPRODUCTIVE RANGE FINDING STUDIES ON  
OCTAMETHYLCYCLOTETRASILOXANE (OMCTS, D<sub>4</sub>) IN MALE  
AND FEMALE SPRAGUE-DAWLEY RATS

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96 FEB 15 AM 11:12

## **Executive Summary:**

An initial preliminary range finding inhalation reproductive toxicity study was conducted to determine effects, if any, on reproduction in Sprague-Dawley rats in a single generation. Both male and female (20/sex/exposure level) rats were exposed to D<sub>4</sub> vapor at 70 and 700 ppm six (6) hours per day for twenty eight (28) days prior to mating; a concurrent filtered air control followed a similar regimen. Exposure was then continued throughout a two week mating phase until necropsy (exposure of female rats was temporarily suspended from gestational day 21 through lactation day 4). Pups were exposed following a similar regimen after weaning on postnatal day 21 through postnatal day 28. Following this initial range-finding study, a repeat range-finding study was conducted because the initial results were equivocal, making interpretation difficult. The repeat range-finding study utilized one group of rats exposed to D<sub>4</sub> vapor at 700 ppm and two filtered air control groups (22/sex). The design of the repeat study was identical to the initial study with the following exceptions:

- a) the pups in the F1 generation were euthanized on postnatal day 4 instead of postnatal day 28,
- b) testicular and epididymal sperm counts and sperm production rates were measured, and
- c) testes, epididymides and ovaries were weighed and examined histologically.

In the initial range-finding study, no significant clinical signs of toxicity were noted in D<sub>4</sub> exposed males or females. Inhibition in body weight gain and food consumption in the 700 ppm exposed female group was observed. This was particularly evident in the females during gestation. There were no adverse effects in overall reproductive performance in D<sub>4</sub> exposed animals (male or female fertility index, pregnancy rate, mating behavior, females with viable pups, gestational period or mean pre-coital intervals). No abnormalities were observed in any of the pups. However, we did observe an apparent reduction in the mean viable litter size (11.6 pups/litter) in the 700 ppm exposure group only. While this observation was statistically significant ( $p < 0.01$ ) when compared to concurrent controls, the control group had an atypically high (based on historical control data) mean viable litter size (16.4 pups compared to an historical range of 11.7–15.9) which was outside the range of normal control data. The mean viable litter size of 11.6 pups/litter in the 700 ppm D<sub>4</sub> group, approximating the lower end of historical control data for this strain of rat, when coupled with the fact that all other reproductive performance indicators were unaffected by exposure to D<sub>4</sub>, confounds interpretation of these data.

In an attempt to ascertain whether or not D<sub>4</sub> could have an impact on mean viable litter size, a second inhalation reproductive study was conducted as

described above. The effects of 700 ppm D<sub>4</sub> exposure on parental body weight gains and food consumption were confirmed in the second study. Again, the inhibition of body weight gain was particularly evident in the D<sub>4</sub> exposed females during gestation. The second study reconfirmed the lack of effect of D<sub>4</sub> exposure on overall reproductive performance (male or female fertility index, pregnancy rate, mating behavior, females with viable pups, or pre-coital interval). Sperm counts and sperm production rates as well as, morphologic assessment of testes, ovaries and epididymides were unaffected by D<sub>4</sub> exposure. However, a statistically significant ( $p < 0.01$ ) reduction in mean viable litter size (8.7 vs. controls of 14.6 and 13.2) was observed as was a statistically significant reduction in the mean number of implantation sites (10.8 vs. controls of 14.6 and 15.8) in the 700 ppm D<sub>4</sub> group. Additionally, pup viability was reduced on day 1 and day 4 of lactation. No gross or visceral abnormalities were observed in either dams or pups exposed to D<sub>4</sub>.

#### **Actions:**

Although we do not believe the results of these preliminary range-finding studies represent a substantial risk to health or environment, we are reporting them to assure compliance with the letter and spirit of TSCA Section 8(e). The high exposure levels used in these studies greatly exceed any human exposures and the experimental results described above represent a potential worst case exposure scenario for examining reproductive outcomes in animals. Nevertheless, as part of Dow Corning's comprehensive Product Stewardship Program (PSP), we will inform our employees and key customers of these interim range-finding results on D<sub>4</sub> through a combination of face-to-face meetings and written material.

In the results described above both males and females were exposed to high levels of D<sub>4</sub> vapor for 28 days prior to mating, during mating and female exposure continued during lactation until weaning. The absence of any significant signs of toxicity and the lack of effect on reproductive organs and on overall reproductive performance is noteworthy. Importantly, in two prior teratology studies on D<sub>4</sub> previously submitted to EPA, one in rats and one in rabbits, there were no effects on mean litter size or on the number of implantation sites.

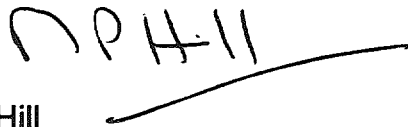
In an attempt to ascertain whether or not there is a gender specific effect or if exposure to both males and females is necessary to produce the smaller mean litter sizes and reduced number of implantation sites observed in the range finding work, much larger dose-response studies are in progress. In these ongoing new studies, we will examine sex specificity in reproductive outcomes by mating treated males with untreated females and visa versa following 70 days of exposure to either 0, 70, 300, 500 or 700 ppm of D<sub>4</sub> vapor. Until these studies

completed, a scientific assessment of the potential effects of high levels of D<sub>4</sub> vapors on reproductive outcomes in animals is not possible.

Dow Corning will inform the Agency of any new pertinent information that may be developed concerning D<sub>4</sub> and will provide EPA with a copy of the final reports of the studies described herein.

If you have any questions concerning the aforementioned studies, please contact Dr. Richard W. Mast, Scientific Director, Product Safety and Toxicology at 517-496-8569. If you require further general information concerning this notification, please contact Dr. Rhys G. Daniels, Regulatory Specialist, Product Safety and Regulatory Compliance at the address provided below or by telephone at 517-496-4222.

Sincerely,

A handwritten signature in black ink, appearing to read "M P HILL", with a long horizontal line extending to the right.

Michael P. Hill  
U.S. Area Vice President  
Director of Health and Environmental Sciences  
(517) 496-4059

**Best Available Copy**